# THE RATES OF ABSORPTION OF RADIO-SODIUM IN NORMAL HUMAN SUBJECTS*

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Communicated June 7, 1937

The internal admistration of radio-sodium in the form of sodium chloride was first performed at the University of California Hospital in March of 1936 upon a subject with lymphatic leukemia. The radioactivity of the patient and his excreta was observed in addition to any possible clinical responses. A second patient with a myelogenous leukemia received the same substance, but of considerably greater activity. No definite clinical improvement or toxic effects were observed; but data referable to the concentration of the radio-sodium in the body fluids and its excretion were obtained from these studies and are reported elsewhere.[1]

Following the intraduodenal administration of the radio-sodium to the second patient it was found that for the succeeding 8 hours the measured activity of his body was greater than was to be expected, allowing for the gamma radiation absorbed by the tissues and the amount of radio-sodium lost by excretion. Recently a third patient, suffering from a reticulum-cell sarcoma of the cervical lymph nodes, was given the activated salt by mouth and the same phenomena were observed for a period of 13 hours.[2] This apparently anomalous behavior of the radio-sodium when given by mouth or by duodenal tube, as contrasted to the results obtained after intravenous administration, was thought to be due to the fact that it was more slowly absorbed than might be expected. This problem has been investigated further by studies concerning the apparent rates of absorption of radio-sodium in normal human subjects.

*Preparation of the Radio-Sodium.*—The radio-sodium was prepared by the deuteron bombardment of crystalline sodium caloride using the magnetic resonance accelerator which was developed by Lawrence and Livingston[3] and later re-designed by Lawrence and Cooksey[4] of the Radiation Laboratory of the University of California at Berkeley. This apparatus, commonly described as the "Cyclotron," has been constructed for the multiple acceleration of light ions to high speeds. The deuterons spiral around within a drum-shaped chamber lying between the poles of a powerful electromagnet. The combined action of the magnetic field and a high frequency oscillating electric field upon these particles produces progressive increments of velocity with every revolution of the ions within the chamber so that their terminal energy upon emerging at the periphery is in the neighborhood of 6,000,000 electron volts. These rapidly moving particles, which consist of a proton and a neutron bound together and are isotopes of ordinary hydrogen ions, stream out of the cyclotron as a narrow beam which is directed against the substance to be activated. When one of these particles approaches the nucleus of a sodium atom the proton is repelled by the intensely positive field and the neutron is captured by the nucleus. The sodium then becomes heavier by the weight of the neutron and its atomic weight increases by one without altering its chemical properties. This isotope of

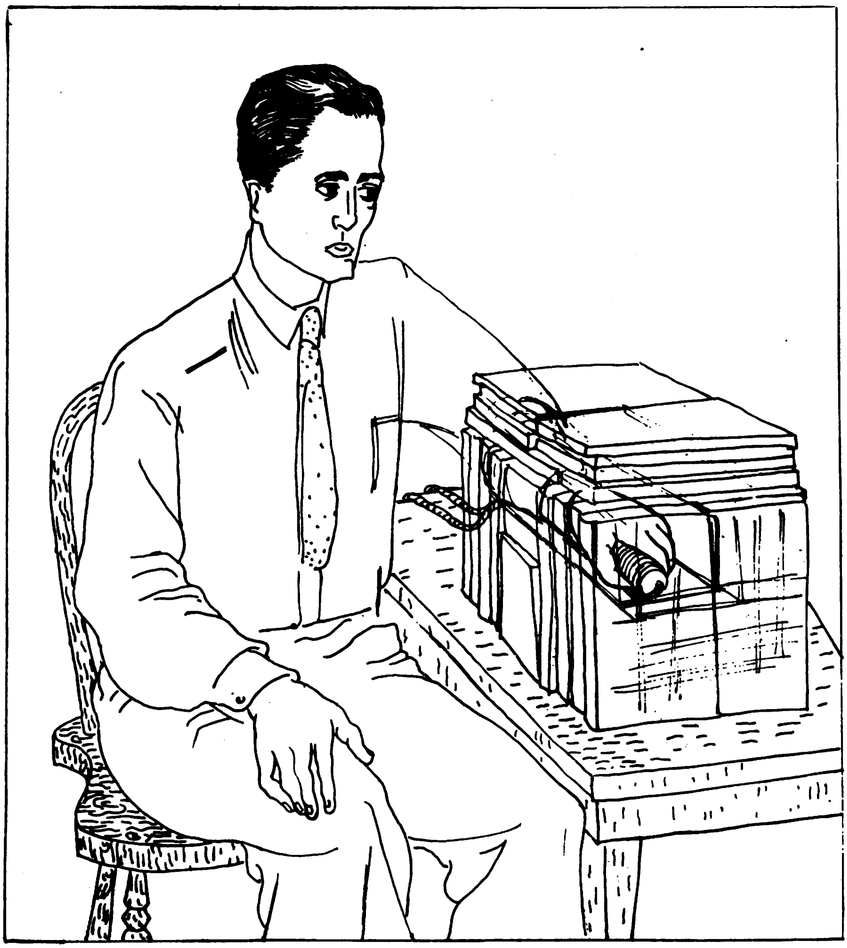

FIGURE 1

sodium does not occur in nature and is unstable; in the course of 14.8 hours, half of its atoms emit an energetic beta ray. When the sodium nucleus loses the electron (i.e., beta ray), magnesium is formed which immediately releases its excess of energy as a gamma ray. These gamma rays enable the investigator to measure quantitatively the amount of radio-sodium in a given sample. The interval of time between the formation of the active magnesium and the emission of its gamma ray is so brief as to be of no consequence, and therefore the distribution of radio-sodium in any biological system can be considered as a measure of the metabolism of the naturally occurring sodium ion. The only possible exception to this view is that the radiations from the activated sodium might alter the function of the organism, or a portion of its cellular components. Colwell,[5] in his excellent monograph, discusses the effect of radiations upon cellular structures and their metabolism. However, the degree of exposure with both beta and gamma rays necessary to accomplish measurable changes was very much greater than was used in the treatment of the previously described patients with radio-sodium. The quantity of the activated salt given to the majority of the subjects in the absorption experiments was from $^1/_{600}$th to $^1/_{1500}$th the amount given to the third patient.

*Method of Study and Administration.*—In the following experiments eight normal human subjects were used, two of them being women. The radioactivity of the hand, after the subject had ingested the radio-sodium by mouth, was used as the "indicator" of absorption. A small hollow lead box with walls of 6 inches in thickness, open at one end and with sufficient space inside to admit the subject's hand and forearm, was used (Fig. 1). This arrangement permits the accurate measurement of very minute quantities of any radioactive substance in the blood and at the same time shields the hand and measuring instrument from the activity of the remainder of the body. A Geiger-Müller counter with a constant voltage supply was used in all of these experiments. The counting chamber was 1 by 4 inches in size and was held in the hand within the lead box. The activity was recorded as impulses per second in the counter circuit.

The radio-sodium was prepared by the deuteron bombardment of from 1 to 2 gm. of crystalline sodium chloride. The sample was then allowed to "age" for at least 90 minutes to permit the decay of the radio-chlorine and then its activity was determined with a quartz fibre electroscope which had been previously calibrated against a 1 mg. mesothorium standard. The salt was then dissolved in a measured amount of water, usually 50 or 100 cc., and then a sufficient amount of the solution measured out so as to give each subject the necessary quantity of radio-sodium to be taken. At the start of each experiment the subject took his station with one hand inside the lead box and the sample to be swallowed in the other, and several background readings were taken. Then the solution was ingested and followed by a glass of water to wash all traces of the radio-sodium out of the mouth and esophagus. Readings from the counter were taken immediately afterward and continued every few minutes for the next hour. A second subject took his place and then drank the activated solution and at the end of the next hour exchanged places with the first individual. In this manner it was possible to carry out these studies upon two subjects at a time. The first few experiments were conducted for a period of from 6 to 7 hours; but since absorption in some instances did not appear to be completed at the end of this time, the later studies were extended to 10 hours.

The first subject received 2000 μc.e.† but it was subsequently found that from 80 μc.e. to 200 μc.e. would give just as satisfactory results. Whenever possible the subjects were in the fasting state for at least 4 hours before taking the radio-sodium. However, it was observed that the taking of food an hour or so before the experiment made no appreciable difference. During the course of the experiments a short period was allowed for the subjects to partake of a light meal and, in this instance as well, no alteration

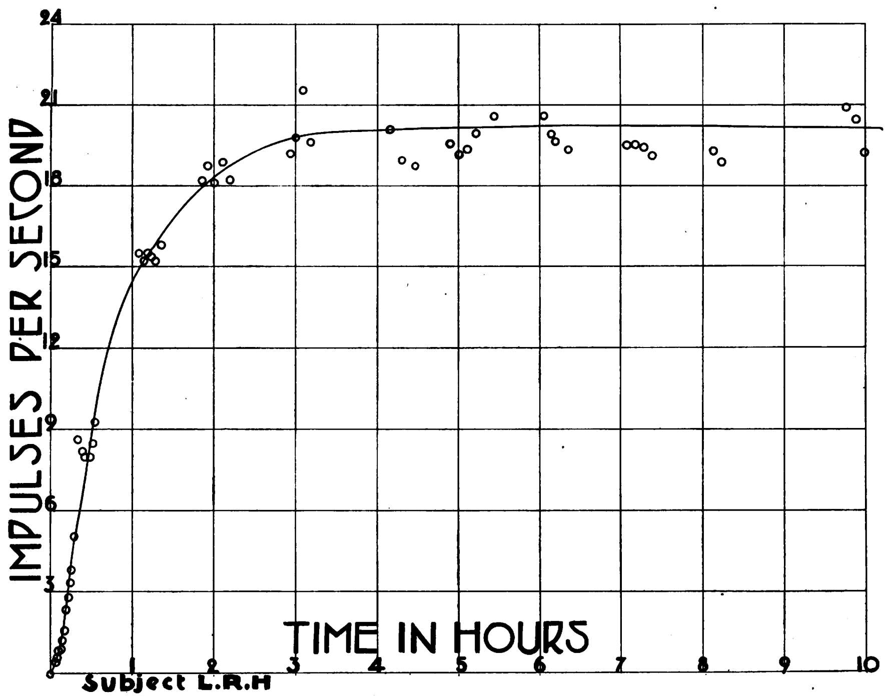


FIGURE 2

in the absorption curves was to be noted. The studies were on the top floor of a large building, and when a subject walked rapidly up the four long flights of stairs from the ground floor a definite but brief increase in the activity of his hand was observed.

Six subjects received the radio-sodium but once and the remaining two took the salt twice. The absorption curves of the individuals receiving the radio-sodium a second time were no more similar upon the second study than the curves of the different subjects.

Two typical absorption curves are shown in figures 2 and 3; the abscissa represents the intervals of time following the ingestion of the radio-sodium and the ordinate the impulses of the counter circuit per second after correction for the decay of the radio-sodium has been made. The interval of time following the taking of the radio-sodium, but before any definite activity could be detected in the hand, varied from $2^1/_2$ to 9 minutes. In figure 2 the initial portion of the curve is quite steep but at the end of 3 hours it becomes flat, suggesting that absorption was completed at the end of this period of time. The beginning of the second curve shown in figure 3 is less sharply inclined, but at the end of 10 hours it has not become level. This gradual increase of activity at the termination of the experiment has

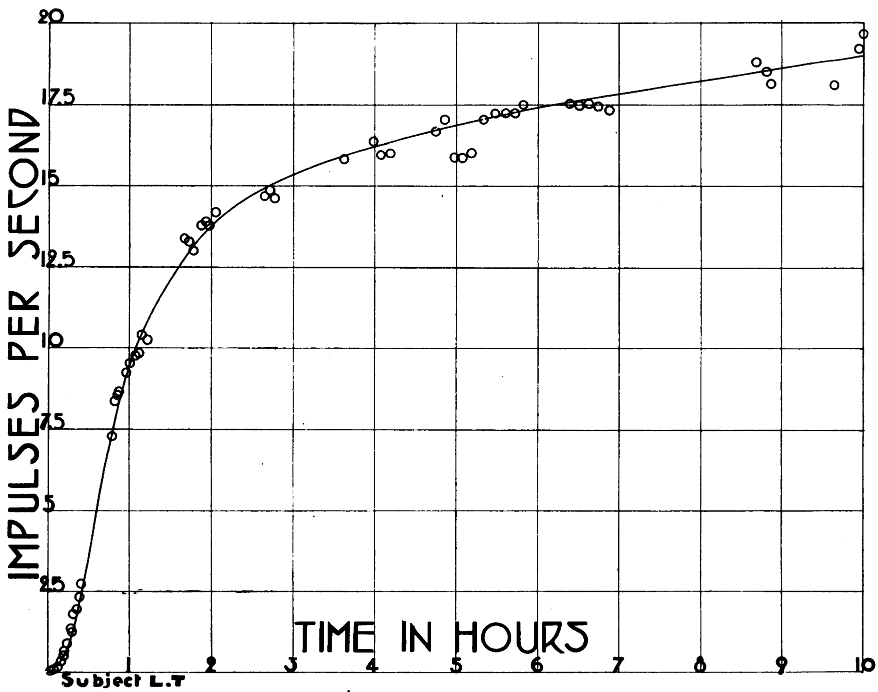


FIGURE 3

been observed in several other subjects but does not appear to be related to the slope of the initial part of the absorption curve. In future studies the period of observation is to be prolonged until absorption has been completed in all the subjects studied.

*Discussion.*—Before any conclusions can be drawn, several factors must be considered. The results are merely the successive measurements of the radioactivity of the subjects' hands. In other words, the hand is an "indicator" of absorption, but not necessarily a quantitative index of the rate that the radio-sodium passes from the digestive tract into the blood stream. The hand is a complex structure composed of many histological entities and into these tissues the atoms of radio-sodium diffuse from the blood. If the rate of diffusion is rapid in the hand then the counter will, in effect, measure the rate of change in activity of the incoming blood stream. However, if the rate of diffusion is slow, in comparison to the rate of absorption, the initial portion of the curve will be flatter and the interval of time before the maximum rise occurs will be prolonged. Alteration of the caliber of the blood vessels will change the total volume of blood in the hand and thereby produce variations in the measurements. An example of this factor was observed following exertion in one of the subjects, and has been previously described. To avoid this source of error the subjects were not exposed to any undue temperature changes and the activity determinations were made only when they were at rest. The possible influence from the accumulation of sweat from the subjects' hands upon the counter tube was determined at the conclusion of several experiments and was found to be negligible.

The rate of diffusion of the radio-sodium into the tissues and their fluids of the remainder of the body may also affect the apparent rate of absorption. If diffusion is rapid this variable can be overlooked; but if it should be slower, yet faster than the rate of absorption, the observed curves will rise more gradually to a maximum. Should the rate of diffusion be slower than absorption then the curve would soon decline after reaching a maximum as the radio-sodium in the blood stream was being taken up by the tissue fluids. Another possible variable is the state of sodium "excess" and "deficit" of the subject at the time when the activated salt is taken. It is reasonable to suppose that the rate of absorption would be more rapid in an individual in a state of sodium "deficit." The influence of loss of the radio-sodium from the body through the various channels of excretion is of no importance during the length of time that these experiments were conducted. The rate of excretion of radio-sodium when given to patients has been found to be less than 0.2 per cent per hour and so the amount lost at the end of 10 hours would be less than the experimental limits of error.

A consideration of the possible factors which might produce significant alterations in the observed rates of absorption leads to the conclusion that the most important variables are the quantity of sodium in the body at the time of experimental study and the rate of diffusion of sodium from the blood stream into the other body structures. Very little is known about the first factor; but it is generally assumed that practically all of the body's sodium is contained in the body fluids, which comprise about 20 per cent of the total body weight, and that diffusion is rapid. Even less information is available as to the effect of the total quantity of sodium in the body upon the rate of absorption. The latter factor can be eliminated as a source of error by placing the subjects upon a fixed sodium intake for a period of time, and after they are in a state of sodium "balance" (i.e., sodium intake equals sodium excretion) for several days, determining the rates of absorption. At present it is not possible to determine the rates of diffusion in normal human subjects; but future studies are planned in conjunction with further clinical investigations upon the metabolism of sodium following administration of radio-sodium to leukemic patients at the University Hospital in the attempt to obtain more precise information upon this question.

*Summary.*—1. The rate of absorption of sodium has been studied following the oral administration of its radioactive isotope to normal human subjects.

2. Absorption of the radio-sodium has been observed to begin within a few minutes and is apparently completed in a period of from 3 to 10 hours in some subjects, but in others equilibrium was not reached at the end of 10 hours.

3. A new method of study of the metabolism of sodium has been described. This technique may be adapted to other artificially radioactive elements, or their compounds, when given by mouth or by other channels of administration.

*Acknowledgment.*—The author wishes to express his appreciation to Dr. Robert S. Stone of the Department of Roentgenology for his encouragement and advice, and to the individuals whose willing coöperation as experimental subjects made this work possible. The radio-sodium was supplied through the courtesy of Prof. Ernest O. Lawrence and his coworkers of the Radiation Laboratory of the University of California and through the support of the Josiah Macy, Jr., Foundation.

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† Microcurie equivalents.

[1] Hamilton, J. G., and Stone R. S., "The Intravenous and Intraduodenal Administration of Radio-Sodium," *Radiology*, **28**, February, 178 (1937).

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[3] Lawrence, E. O., and Livingston, M. S., *Phys. Rev.*, **40**, April, 19 (1932).

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